

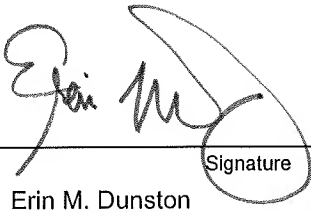
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PRE-APPEAL BRIEF REQUEST FOR REVIEW		Docket Number (Optional)	
<p>I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)]</p> <p>on _____</p> <p>Signature _____</p> <p>Typed or printed name _____</p>		Application Number	Filed
		09/901,782	July 9, 2001
		First Named Inventor	
		Susan HARDIN	
		Art Unit	Examiner
		1634	Bradley L. SISSON
<p>Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.</p> <p>This request is being filed with a notice of appeal.</p> <p>The review is requested for the reason(s) stated on the attached sheet(s). Note: No more than five (5) pages may be provided.</p>			
<p>I am the</p> <p><input type="checkbox"/> applicant/inventor.</p> <p><input type="checkbox"/> assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)</p> <p><input checked="" type="checkbox"/> attorney or agent of record. Registration number 51,147</p> <p><input type="checkbox"/> attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____</p>		<p> Signature</p> <p>Erin M. Dunston Typed or printed name</p> <p>(703) 836-6620 Telephone number</p> <p>November 26, 2010 Date</p>	
<p>NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.</p>			

☒ *Total of 1 forms are submitted.

This collection of information is required by 35 U.S.C. 132. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of)	MAIL STOP AF
Susan HARDIN <i>et al.</i>)	Group Art Unit: 1634
Application Serial No.: 09/901,782)	Examiner: Bradley L. Sisson
Filing Date: July 9, 2001)	Confirmation No.: 9388
Title: COMPOSITIONS FOR REAL-TIME)	MAIL STOP AF
NUCLEOTIDE SEQUENCE)	
DETERMINATION)	

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Commissioner for Patents
P.O. Box 1450; Alexandria, Virginia 22313-1450
Sir:

Applicants hereby request a pre-appeal brief review pursuant to the program announced on June 20, 2005, as reported in the Official Gazette on July 12, 2005.

Claim Rejections Under 35 U.S.C. § 103

Pending Claims 10, 16-18, 50, 51, 53-55, 64, 65, 67-69, 71, 72, 74, 76, 77, 79-82, 84-87, 89-92, 95-98, 100, 102-106, and 108-11 were rejected under 35 U.S.C. § 103(a) as purportedly obvious over U.S. Patent No. 6,982,146 to Schneider *et al.* ("Schneider") in view of U.S. Patent No. 7,037,687 to Williams *et al.* ("Williams *et al.*") and U.S. Patent No. 6,306,607 to Williams ("Williams"). *See Final Office Action mailed May 28, 2010, Pages 5-11, ¶¶ 9-32.* These rejections are respectfully traversed at least because Schneider and Williams cannot be combined as the Examiner suggests because their teachings are incompatible and the proposed combination would result in an inoperable method. Under established precedent, such a combination cannot support an obviousness rejection.

"A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a).

Underlying factual determinations in an obviousness analysis include (1) the scope and content of the prior art, (2) the level of ordinary skill in the art, (3) the differences between the claimed invention and the prior art, and (4) objective indicia of nonobviousness. *Merck & Co. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1369 (Fed. Cir. 2005) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966)).

Applicants respectfully submit that a *prima facie* case of obviousness against Claims 10, 16-18, 50, 51, 53-55, 64, 65, 67-69, 71, 72, 74, 76, 77, 79-82, 84-87, 89-92, 95-98, 100, 102-106, and 108-111 due to Schneider in view of Williams *et al.* or Williams has not been made.

It is important to recognize that each of Claims 10, 16-18, 50, 51, 53-55, 64, 65, 67-69, 71, 72, 74, 76, 77, 79-82, 84-87, 89-92, 95-98, 100, 102-106, and 108-111 must be considered *as a whole*. See, e.g., *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1742 (2007) ("What matters is the objective reach of the claim."); *Datascope Corp. v. SMEC, Inc.*, 776 F.2d 320, 324 (Fed. Cir. 1985) (noting that the references must be considered "as a whole" and that the claimed subject matter must be considered "as a whole."). Considering each of Claims 10, 16-18, 50, 51, 53-55, 64, 65, 67-69, 71, 72, 74, 76, 77, 79-82, 84-87, 89-92, 95-98, 100, 102-106, and 108-111 as a whole is important because "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 127 S. Ct. at 1741. That is because "inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *Id.*

Applicants respectfully submit that only by using impermissible hindsight would

one modify Schneider, Williams *et al.*, and Williams as the Examiner suggests to arrive at Applicants' Claims 10, 16-18, 50, 51, 53-55, 64, 65, 67-69, 71, 72, 74, 76, 77, 79-82, 84-87, 89-92, 95-98, 100, 102-106, and 108-111. Yet, factfinders must avoid the distortion caused by hindsight bias "and must be cautious of arguments reliant upon *ex post* reasoning." *KSR*, 127 S. Ct. at 1742 (citing *Graham* and "warning against a 'temptation to read into the prior art the teachings of the invention in issue' and instructing courts to 'guard against slipping into the use of hindsight.'").

The principle of operation of Schneider is a FRET interaction between a donor on a polymerase and an acceptor on a nucleotide. However, the Examiner admits that Schneider does not teach that the fluorescent label is released from the nucleotide by action of the polymerase (see *Final Office Action* mailed May 28, 2010, Page 8, ¶ 23) and that neither Schneider nor Williams *et al.* have been found to disclose using a nucleotide where the fluorescent label is attached to a terminal phosphate. See *Final Office Action* mailed May 28, 2010, Page 9, ¶ 28.

Williams is alleged to teach a nucleotide comprising a label attached to a terminal phosphate. However, that is not a complete description of the teachings of Williams. Williams only teaches nucleotides comprising a fluorophore attached to the γ -phosphate that also comprise a quencher moiety. See *Williams at Abstract; at Column 3, Lines 36-58*. The principle of operation of Williams is detection of the fluorescent label after it is released from the quencher.

Thus, the principle of operation of the method of Schneider is incompatible with the principal of operation of the method by Williams. ***Combination of each with the other would defeat the principle of both.*** The presence of the quencher moiety of

Williams nucleotides would defeat the principle of FRET transfer between the donor and acceptor in the method described by Schneider. Modification of the Williams nucleotides to remove the quencher moiety would render the nucleotides unsuitable for their intended purpose. Because of this, one of ordinary skill in the art, prior to Applicants' invention, would not have modified Schneider and Williams as the Examiner suggests.

If a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. The Federal Circuit's comments in *McGinley v. Franklin Sports, Inc.*, are instructive:

We have noted elsewhere, as a "useful general rule," that references that teach away cannot serve to create a prima facie case of obviousness. *In re Gurley*, 27 F.3d 551, 553, 31 USPQ2d 1130 (Fed. Cir. 1994). ***If references taken in combination would produce a "seemingly inoperative device," we have held that such references teach away from the combination and thus cannot serve as predicates for a prima facie case of obviousness.*** *In re Spinnoble*, 405 F.2d 578, 587, 160 USPQ 237, 1244, 56 C.C.P.A. 823 (1969) (references teach away from combination if combination produces seemingly inoperative device); *see also In re Gordon*, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984) (inoperable modification teaches away).

McGinley v. Franklin Sports, Inc., 262 F.3d 1339, 1353-54 (Fed. Cir. 2001) (emphases added); *see also Tec Air, Inc. v. Denso Mfg. Michigan Inc.*, 192 F.3d 1353, 1360 (Fed. Cir. 1999) (noting that there "is no suggestion to combine, however, if a reference teaches away from its combination with another source" and that "[i]f when combined, the references 'would produce a seemingly inoperative device,' then they teach away from their combination."). Removal of the quencher moiety from the Williams

nucleotides would be contrary to the principle of operation taught in Williams and would render the nucleotides unsatisfactory for their intended purpose.

Thus, either way one considers the proposed combination of Schneider and Williams, there could not have been any motivation to modify the publications as would be required to make the proposed combination. Williams *et al.* has not been alleged and does not cure the deficiencies of Schneider and Williams.

Because a *prima facie* case of obviousness against Claims 10, 16-18, 50, 51, 53-55, 64, 65, 67-69, 71, 72, 74, 76, 77, 79-82, 84-87, 89-92, 95-98, 100, 102-106, and 108-111 based upon Schneider, Williams *et al.*, and Williams has not been made, Applicants respectfully request withdrawal of the 35 U.S.C. § 103(a) rejection thereof.

Conclusion

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

The Director is hereby authorized to charge any appropriate fees under 37 C.F.R. §§ 1.16, 1.17, 1.20(d), and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

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Respectfully submitted,
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